



**THE 2ND MEMORIAL LECTURES FOR ESTABLISHMENT OF
INTERNATIONAL ACADEMIC COOPERATION RELATIONSHIP BETWEEN
FACULTY OF AGRICULTURE, SHINSHU UNIVERSITY, JAPAN &
ZHEJIANG ACADEMY OF AGRICULTURAL SCIENCES, CHINA**

PROF JIANZHI PAN, ZAAS

PROF TOSHIO OSHIDA, AZABU

PROF TAKAAKI KOBAYASHI, NAGOYA

DR TAKAHIRO TAGAMI, NILGS

DR YOSHIKAKI NAKAMURA, NIBB

ASSIST PROF MISATO UEHARA, SHINSHU

NOVEMBER 20, 2012

FACULTY OF AGRICULTURE, SHINSHU UNIVERSITY





The 2nd Memorial Lectures for Establishment of
International Academic Cooperation Relationship between
Faculty of Agriculture Shinshu University, Japan &
Zhejiang Academy of Agricultural Sciences, China

Date: November 20, 2012

Venue: Faculty of Agriculture, Shinshu University

Host: Faculty of Agriculture, Shinshu University

Executive Committee:

President: The University Vice President & Dean,

Professor Soichiro Nakamura

Chairman: Professor Hiroshi Kagami

Vice Chairman: Professor Koh-ichi Hamano

Member: Professor Tamao Ono

Member: Professor Kohzy Hiramatsu

Member: Professor Kiyoshi Banno

Member: Professor Hiroshi Fujii

Member: Associate Professor Yuji Takagi

Member: Associate Professor Takeshi Shimosato

Member: Assistant Professor Shinichi Yonekura

Member: Assistant Professor Takeshi Kawahara

Member: Assistant Professor Masaki Ihara

Member: Assistant Professor Takafumi Watanabe

Member: Assistant Professor Misato Uehara

Member: Assistant Professor Shigeru Katayama

Message from the President



Soichiro Nakamura, Ph.D., Professor
President of The SHINSHU-ZAAS Memorial Lectures
Vice President and Dean, Shinshu University

An agreement for the academic cooperation and exchange with an expectation was successfully made and concluded between the Faculty of Agriculture, Shinshu University, Japan and Zhejiang Academy of Agricultural Sciences (ZAAS), the People's Republic of China, on the 12th of September 2012. This is the second memorial meeting marking the conclusion of the academic cooperation and exchange agreement.

On the opening of the memorial lectures, on behalf of Shinshu University and on my personal behalf, I would like to express a sincere gratitude and give a hearty welcome to all the participants, and special thanks to the guest speaker, Professor Jianzhi Pan, Institute of Animal Husbandry and Veterinary Sciences in ZAAS. As an additional remark, we would not have this occasion if it wasn't for the networking Professor Kagami of Shinshu University has made globally over the years of his work. I would like to express my greatest respect for Dr. Kagami both as a human being and as a scientist. Anyway, I hope that the cooperation and exchange in academic areas of mutual interests would bring fruitful results for the advancement of research, education and international understanding between the parties.

As you would realize, the speakers we have here are all leading researchers who are active in the area of fundamental animal bioscience or livestock science. We would like to invite the speakers to not only share with us the results of their basic research but also effort towards transferring technology to corporations, its advantages and disadvantages, as well as topics on regional development *via* animal biotechnology and views on sustainability for the future. I am confident that their lectures will help to raise awareness in participants and inspire the younger generations, which will then lead to the advancement of science and technology globally.

In this memorial meeting, I am looking forward to productive discussions, and anticipate that many fruitful conclusions will generate a new phase to construct international networks for the modern science and biotechnology. I hope, we exchange scientific information with one another to deepen the mutual understanding, and incubate international co-operative relationships. Lastly, taking this opportunity, I thank you all for the assistance for the conclusion of the academic cooperation and exchange agreement between the parties as well as in the preparation of this second memorial meeting.

Thank you all for your warm attention.

November 20, 2012.
Soichiro Nakamura

Message from the Chairman



Hiroshi Kagami, Ph.D., Professor
Chairman of The SHINSHU-ZAAS Memorial Lectures
Fac Agriculture, Shinshu University

On behalf of the Organizing Committee and Shinshu University, I would like to welcome cordially all delegates and accompanying persons to the 2nd Memorial Lectures for Establishment of International Academic Cooperation Relationship between Faculty of Agriculture Shinshu University, Japan & Zhejiang Academy of Agricultural Sciences, China. On the 12th of September 2012, an agreement for the academic cooperation relationship was successfully made between Shinshu and ZAAS. The agreement could not be made without strong leaderships and initiatives of Professor Soichiro Nakamura; The Vice President & Dean, Shinshu University, Japan, and Professor Meng Zhiqi; The Vice President, ZAAS, China. Also, great efforts and enthusiasm by Professor Jianzhi Pan was contributed for the agreement.

To celebrate the international agreement, first Memorial Lectures was successful conducted in ZAAS. It is our great honor to host the second Memorial Lectures in our campus. Recently, many academic findings and research strategies have been obtained in basic and applied biological sciences. These progress would open up new frontier for sustainable agricultural development and biomedical sciences. During this memorial lectures, leading scientists from internationally qualified institutions; ZAAS, AZABU, NAGOYA, NILGS, NIBB, will talk on their latest finding on animal biotechnology and their industrial applications. Also, contribution of the biotechnology to quality of life & spiritual happiness in human being will be discussed by a promising scientist from SHINSHU. Global pollution and food shortage against the comfortable environment would be one of the most important subjects to be overcome by the wisdom of the academic findings.

We believe their impressive lectures with fruitful discussion would make this memorial lectures very successful. Also, the interaction of leading scientists and undergraduate & graduate students will activate the academic achievements. I wish this memorial lectures will be the beginning of epoch for mutual aspects.

Thank you very much for participating this memorial lectures.

Yours sincerely,

November 20, 2012.

Hiroshi Kagami

SCIENTIFIC PROGRAM

&

**ABSTRACTS FOR
MEMORIAL LECTURES**

Opening Address

Chairman: Professor Hiroshi Kagami

14:30-14:40

Professor Soichiro Nakamura, The University Vice President & Dean

Memorial Lecture 1

Chairman: Associate Professor Yuji Takagi

14:40-15:10

Challenges and Opportunities for Animal Research and Production in China

...Professor Jianzhi Pan (Zhejiang Academy of Agricultural Sciences, China)

Memorial Lecture 2

Chairman: Associate Professor Yuji Takagi

15:10-15:40

Unknown Aspects on Animal Production – How Animal Production Associated with the People?

...Professor Toshio Oshida (Faculty of Veterinary Medicine, Azabu University)

Memorial Lecture 3

Chairman: Assistant Professor Shinichi Yonekura

15:40-16:10

Xenotransplantation Using Genetically Modified Pigs: Current Status and Progress Towards Clinical Application

... Professor Takaaki Kobayashi (School of Medicine, Nagoya University)

Coffee Break

16: 10-16:30

Memorial Lecture 4

Chairman: Professor Tamamo Ono

16:30-17:00

Sex Differentiation of Primordial Germ Cells in Chicken Embryo

...Senior Researcher Dr. Takahiro Tagami (National Institute of Livestock and Grassland Science)

Memorial Lecture 5

Chairman: Professor Kohzy Hiramatsu

17:00-17:30

Germ-Cell Transplantation in Chicken and Mice

...NIBB Research Fellow Dr. Yoshiaki Nakamura (National Institute for Basic Biology)

Memorial Lecture 6

Chairman: Assistant Professor Shigeru Katayama

17:30-18:00

Better Landscape, Better Life

... Assistant Professor Misato Uehara (Faculty of Agriculture, Shinshu University)

Closing Address

18:00-18:10

Professor Hiroshi Kagami, Chairman of The Memorial Lectures

Commemorative Photo

18:10-18:20

Dinner Party

18:30-20:30



Challenges and Opportunities for Animal Research and Production in China

Jianzhi Pan, Ph.D.

**Professor & Assistant Director, Zhejiang Academy of Agricultural Sciences (ZAAS)
Hangzhou, Zhejiang, China**

China is now the biggest producer of major livestock products. Especially, the output of meat and eggs ranks first in the world. In recent 30 years, animal production in China increased rapidly with 7.8%, 10.3% growth rate for meat or egg every year. The model of animal production is also changing to industrial systems. It is forecasted that China's consumption of meat products will continue to climb sharply due to a rising population, strong growth in per capita income and shifting consumption patterns. However, productivity of animal production was still far below the developed countries. Some difficulties and problems still existed, such as low industrialization level, poor quality and safety of animal products, insufficient feed resources and lower feed utilization etc. How to solve the difficulties and problems have been major tasks for the Chinese investigators and producers. To promote animal production to that of international standard, and meet different hierarchies of consumptions demand, China's animal husbandry needs to transform the way of development from extensive one to intensive one, and have to take into account the balance of the quality, safety and productivity. We must vigorously promote overall research on animal science and technologies, especially for genomics and molecular breeding, modern reproduction techniques, feed nutrition, disease prevention and food safety.

C. V.

1989.7. Graduated from Zhejiang Agricultural University, China (B. Sc.)
1989. 8. Research Assistant at the ZAAS, China
1992.2. Graduated from Zhejiang Agricultural University (M.S.)
1994.9. Assistant researcher at the ZAAS, China
2000.3. Graduated from Gifu University (Ph. D.)
2000.4. Postdoctoral Researcher at Shizuoka University.
2002.4. Collaborative Researcher, at BioResource Center, RIKEN
2007.4. Senior Research Scientist at BioResource Center, RIKEN
2009.4. Professor at the ZAAS, China
2012.7. Assistant Director of Institute of Animal Science at the ZAAS, China



Unknown Aspects on Animal Production - How Animal Production Associated with the People?

**Toshio Oshida, V.M.D., Ph.Ds. in V.M., Agr., Eng.
Professor, Faculty of Veterinary Medicine, Azabu University
Fuchinobe, Kanagawa, Japan**

In recorded history, human being has been associated with animals and obtained many benefits. Animal production images pig or glassland farm. However, many people can not feel further association with the animal production. Watching the animal production in a viewpoint to know how there is the thing which oneself eats every day would make strongly familiar for the subjects as the mean of a food supply. For example, "Why chickens lay eggs every day? How big the animals can the grow? Why pregnant animals can more lactate? What meats can be eaten as raw? Why dairy milk can not be sold in pet bottle?. When is asked these question, few can be answered correctly. Reflect, how much things to understand in one's life for food. And It can be considered that the interests about the meal gradually rises when one of these problems is settled. Blow up imagination in being up in one one's point, two points and would like to give a lecture having you realize the need to have intention to know.

"By the way, what shall we have for today's dinner?"

C. V.

1972. V.M.D. from Faculty of Veterinary Medicine, Azabu University
1977. Ph.D. from Graduate School of Veterinary Medicine, Azabu University
1980. Associate Professor, Faculty of Veterinary Medicine, Azabu University
1997. Professor, Faculty of Veterinary Medicine, Azabu University
2005. Visiting Professor, Shenyang Institute of Applied Ecology, The Chinese Academy of Sciences
President, The Japanese Society of Swine Science
President, The Japanese Society of Animal Hygiene

Research Awards

1993. Research Award of The Japanese Society of Swine Science
2005. Research Award of The Japanese Society of Animal Hygiene
Publication includes many books on Animal Hygiene and Swine Sciences



Xenotransplantation Using Genetically Modified Pigs: Current Status and Progress Towards Clinical Application

Takaaki Kobayashi, M.D., Ph.D.
Professor, School of Medicine, Nagoya University
Tsurumai, Showa, Nagoya, Japan

Although transplantation is now accepted as the only or best treatment for end stage organ failure (such as heart, lung, liver, kidney and pancreas), the growing shortage of donors is one of critical issues. Xenotransplantation using animal organs, tissues or cells was considered to be a promising (and then, ultimate) solution to such a serious problem. Most researchers have attempted to produce genetically modified pigs that would be suitable for transplantation into humans. During these two decades, two “breakthrough” innovations have been developed. One was the production of transgenic pigs expressing hDAF (CD55) to suppress complement activation in 1994. The other was $\alpha 1, 3$ galactosyltransferase gene knockout (GTKO) to eliminate the major xenoantigens, Gala1,3Gal (aGal) antigens, using cloning technology in 2002.

However, to date, longest graft survivals of heart, kidney, liver and lung are 8 months, 3 months, 9 days and 5 days, respectively, though hyperacute rejection could be avoided. It is speculated that “inflammation” and “coagulation disturbance”, which would cause thrombotic microangiopathy and consumptive coagulopathy, are limiting factors in obtaining long-term xenograft survival. Our collaborative group (National Institute of Agrobiological Sciences, Prime Tech LTD and Nagoya University School of Medicine) and other groups have recently produced cloned pigs expressing human thrombomodulin (hTM) that has anti-coagulant and anti-inflammatory function. In addition to GTKO, complement regulatory proteins (CD46, CD55, CD59) and hTM, many genetically engineered pigs have been produced around the world, which express CD39, TFPI (Tissue Factor Pathway Inhibitor), EPCR (endothelial protein C receptor), HO-1, A-20, TNFRI-Fc, CTLA4-Ig, CD47, HLA-E, CIITA-DN, LEA29Y, TRAIL, Fas-L and shRNA against PERV gene. Furthermore, the production of humanized pig organs has also been attempted in combination with regenerative medicine. At present, organ xenotransplantation is still in the preclinical stage.

On the other hand, cell xenotransplantation such as pancreatic islet (for type 1 diabetes) and neuronal cell (for Parkinson’s disease) showed considerable progress. Pig islet graft survival for over 6 months in non-human primates has been reported by several institutes. Clinical trial of pig islet transplantation authorized by New Zealand government is now being undertaken.

It is essential to settle the issue of infection and regulation. The first and second WHO global consultation on regulatory requirements for xenotransplantation clinical trials were held at Changsha (China) in 2008 and at

Geneva (Switzerland) in 2011, respectively. To promote the sound clinical trial, global cooperation system will be established by International Xenotransplantation Association (IXA) in collaboration with WHO. Clinical application of xenotransplantation, which should be justified on the basis of a favorable risk/benefit assessment, will be realized in the not so distant future.

C.V.

1985. Graduated from Nagoya University School of Medicine
1985-1986. Intern, Nishio City Hospital, Nishio
1986-1988. Resident, Department of Surgery, Anjo Kosei Hospital, Anjo
1988-1990. Resident, Department of Gastroenterological Surgery, Aichi Cancer Center Hospital, Nagoya
1990-1991. Clinical Fellow, Department of Transplant Surgery, Nagoya Daini Red Cross Hospital, Nagoya
1991-1993. Clinical Fellow, Department of Surgery II, Nagoya University School of Medicine, Nagoya
1994-1995. Research Fellow, Oklahoma Transplantation Institute, Oklahoma, USA
1995-1999. Medical Staff, Department of Surgery II, Nagoya University School of Medicine, Nagoya
1999-2002. Assistant Professor, Department of Medical Supplies, Nagoya University School of Medicine
2002-2004. Lecturer, Nagoya University School of Medicine
2004-2005. Assistant Professor, International Affairs, Nagoya University Graduate School of Medicine
2005-2007. Assistant Dean, International Affairs, Nagoya University Graduate School of Medicine
2007-2012. Professor, Department of Applied Immunology, Nagoya University School of Medicine
2012- Professor, Department of Transplant Immunology, Nagoya University School of Medicine
2013- President-Elect, International Xenotransplantation Association



Sex Differentiation of Primordial Germ Cells in Chicken Embryo

Takahiro Tagami, D.V.M.

Senior Researcher, National Institute of Livestock and Grassland Science (NILGS), Japan

Tsukuba, Ibaraki, Japan

Germ cells normally have the potential to differentiate into either spermatozoa or ova, depending on their sex. Kagami et al. (1995, 1997) produced mixed-sex somatic chimeric chickens by injecting blastodermal cells, containing PGCs, obtained from stage X embryos (Day 0 embryo) into the same stage of recipient embryos. The donor male or female PGCs derived from stage X could differentiate into functional ovum or spermatozoa in the mixed sex chimeric ovary or testes, respectively. Chicken PGCs derived from stage 15 (Day 2.5), on the other hand, might not differentiate into normal gamete after injection into the opposite sex recipient embryos.

To investigate the differentiation pattern of female PGCs derived from stage 15 (Day 2.5), in male gonads in chickens, three germline chimeric chickens were generated by injecting female PGCs into the male recipient embryos. After these male chimeras reached sexual maturity, the semen samples were analyzed for detecting W-bearing cells by PCR and in situ hybridization analyses. The results indicated that the female PGCs had settled and differentiated in their testes. A histological analysis of the seminiferous tubule in those chimeras demonstrated that the W-bearing spermatogonia, spermatocytes and round spermatids accounted for 30.8%, 32.7% and 28.4%, respectively. However, the W-bearing elongating spermatid was markedly lower (7.7%) as compared to the W-bearing round spermatid. The W-bearing spermatozoa were hardly ever observed (0.2%). It was concluded that although female PGCs in male gonads are capable of passing through the first and second meiotic division in adapting themselves to a male environment, they are hardly complete spermiogenesis. The progeny tests of these germline chimeras clearly indicated that the female PGCs could not differentiate into functional spermatozoa in mature male gonads. The analyses of two kinds of mixed-sex chimeras may have suggested that the irreversible sexual differentiation of chicken PGCs begin between stage X and stage 15.

C.V.

1987-1993 - Hokkaido University, Graduate School of Veterinary Medicine

1993 - Researcher, National Institute of Animal Industry (Japan)

2002 - Senior Researcher, National Institute of Livestock and Grassland Science (Japan)

Research Award

2011.11. NARO prize 2011 (from The National Agriculture and Food Research Organization)



Germ-Cell Transplantation in Chicken and Mice

Yoshiaki Nakamura, Ph. D.

**NIBB Research Fellow, Division of Germ Cell Biology, National Institute for Basic Biology, Japan
Okazaki, Aichi, Japan**

Spermatogonial stem cells (SSCs) and its precursor cells, primordial germ cells (PGCs), can produce viable offspring through the process of differentiation, maturation and fertilization. To date, techniques for transplantation of PGCs and SSCs have been established in several animal species. In combination with transplantation, manipulation of PGCs or SSCs can be used as genetic conservation and genetic modification in animals. However, further development of such applied research using PGCs or SSCs requires the efficiency of obtaining donor-derived progeny to be improved.

Unlike mammals, in avian embryos, PGCs undergo a period of migration using the blood vascular system, and this migration step is suitable for their collection and transplantation. Development of a method for purification of PGCs from embryonic blood has facilitated the production of germline chimeras in chickens (Tajima et al. 1993). However, the germline transmission rate of donor PGCs still remains low because a competition between donor- and recipient-derived germ cells in chimeric gonads occurs. Nakamura et al. (2010a, 2012) demonstrated that the proportion of donor-derived gametes is increased by removal of endogenous PGCs in recipient embryos. Stable production of recipient embryos lacking endogenous PGCs was achieved following the injection of busulfan solubilized in a sustained-release emulsion into the yolk of fertile chicken eggs. This method enabled for the almost complete replacement of a recipient germline following transplantation of donor PGCs in birds. Nakamura et al. (2010b) firstly succeeded to use a limited number of fertilized eggs from a rare chicken breed, Gifu-jidori fowl (a Japanese natural treasure), and achieve the cryopreservation of PGCs and subsequent regeneration of live Gifu-jidori originating from frozen-thawed PGCs via germline chimeras. Now, these technologies are applied to practical germplasm banking in chickens. PGCs from 15 chicken breeds were collected, and these cells have been cryopreserved to date in Naro Institute of Livestock and Grassland Science (NILGS) gene bank (Tsukuba, Japan).

In mammals, manipulation of PGCs is difficult because the development of mammalian embryo is accomplished inside another organism. As an alternative, intra-tubular SSCs transplantation was established in mice (Brinster & Zimmerman 1994). After a single cell suspension of the donor testis is transplanted into the seminiferous tubules of recipients, the injected SSCs will migrate from lumen to basal membrane by passing through the blood-testis barrier between Sertoli cells (homing) and then form spermatogenic colonies that exhibit continual spermatogenesis. This experimental system has prompted the purification of SSCs, and it has been demonstrated that stem cell activity is enriched in undifferentiated spermatogonia (Aundiff) in mice (Shinohara et al. 2000). However, the behavior of donor Aundiff after transplantation is largely unknown. To obtain insight into the behavior of donor Aundiff after

transplantation in mice, continuous observation was conducted using in vivo live-imaging (Yoshida et al. 2007). Migration of donor Aundiff with extend lobopodia was observed in the tubule lumen just after transplantation. This active migration might be involved in Aundiff homing to stem cell niches. The behaviors of donor Aundiff on the basement membrane consists two patterns. Single isolated Aundiff actively migrated with extend lobopodia. By contrast, interconnected Aundiff underwent cell division adjacent to the vascular network. These results first revealed the live SSCs behaviors following transplantation, and the importance of the vasculature pattern for their homing process. At present, I am challenging the mechanisms of homing and spermatogenic colony formation of SSCs in mice to increase the colonizing efficiency of SSCs after transplantation.

C.V.

2006.3. Graduated from Faculty of Agriculture, Shinshu University, B.Sc.

2008.3. Graduated from Graduate School of Agriculture, Shinshu University, M.S.

2011.3. Interdisciplinary Graduate School of Science and Technology, Shinshu University, Ph. D.

2009.4 - 2011.3. JSPS Research fellow (DC2), Japan Society for the Promotion of Science (JSPS)

2011.4 – present. NIBB Research Fellow, Division of Germ Cell Niology, National Institute for Basic Biology (NIBB)

Research Awards

2007.3. Outstanding Presentation Award in the Annual meeting of JPSA
(from Japanese Poultry Science Association)

2008.3. Shinshu University Faculty of Agriculture Award
(from Faculty of Agriculture, Shinshu University)

2009.9. 2009 SRD Outstanding Presentation Award
(from Society for Reproduction and Development)

2009.9. Best Presentation Award in 111th annual Meeting of JSAS
(from Japanese Society of Animal Science)

2010.9. The Journal of Poultry Science Outstanding Paper Award
(from Japanese Poultry Science Association)

2010.9. Best Poster Award in the Czech-Japan Joint Symposium for Animal Reproduction
(from Society for Reproduction and Development)

2011.4. Shinshu University Distinguished Service Award
(from Shinshu University)

2011.7. Shinshu PAFS Award
(from Shinshu Foundation for Promotion of Agricultural and Forest Science)



Better Landscape, Better Life

Misato Uehara, Ph.D.

Assistant Professor, Faculty of Agriculture, Shinshu University

Minamiminowa, Nagano, Japan

Neither frontier science and technology nor the financial theory necessarily enrich the society. An accident of the Fukushima Daiichi Nuclear Power Plant and an economic crisis in the United States and Europe have proven that. On the other hand, Buckminster Fuller and Ian McHarg and Sim Van Der Ryn have insisted on importance of an inclusive design and the best use of the regional tradition in Ecological planning since 1960's. This time, I'd like to think about the relation between an environmental symbiosis technology in the countryside and a beautiful landscape.

C.V.

Kyushu Institute of Design of Environmental design course in 2000 with a Bachelor of Design, Master degree in 2002, Doctor degree in 2005 at the Graduate School of design, the University of Kyushu. This design course (since 1968) is the only systematic faculty of education in national university of Japan.

The holistic Design Science methods were learnt from the specialist of architecture, the city planning, and landscape ecology in environmental design course.

He has research occupation in different field; 1.research assistant of Design, Kobe design University in 2005-2007, under the direction of Prof. Takahito SAIKI(Doctor of Engineering at Tokyo University), 2.Assistant Professor, Faculty of Agriculture, Shinshu University, under the direction of Prof. Kunihiro SASAKI (Doctor of Agriculture at Kyoto University).

He is a generalist with ecological planning in both design and research approaches.



THE SECOND MEMORIAL LECTURES FOR SHINSHU & ZAAS
November 20, 2012